PATENT COOPERATION TREATY

the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

MBM & Co.
Box 809, Station B
Ottawa, Ontario K1P 5P
CANADA

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	03.12.2004
Applicant's or agent's file reference: 335-148PCT	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA 03/01229	19.08.2003	19.08.2002

Applicant: LORUS THERAPEUTICS INC. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 335-148PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/CA 03/01229	International filing date *(day/month/year)* 19.08.2003	Priority date *(day/month/year)* 19.08.2002
International Patent Classification (IPC) or both national classification and IPC A01N43/50		
Applicant LORUS THERAPEUTICS INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 18 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.03.2004	03.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Klaver, J Telephone No. +49 89 2399-8601

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA 03/01229

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-65, 68-72	as originally filed
66, 67	filed with telefax on 20.08.2004

Claims, Numbers

1-27	filed with telefax on 20.08.2004

Drawings, Sheets

1/1	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

   see separate sheet

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	16, 17 (part), 23-26
	No:	Claims	1 - 15, 17(part), 18-22,27
Inventive step (IS)	Yes:	Claims	16, 17 (insofar as novel), 23 - 26
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-15, 18 - 27
	No:	Claims	

2. Citations and explanations

   see separate sheet

I Amendments going beyond the disclosure as filed (Rule 70.2 (c) PCT).

also claims 14, 17, 22

Amended claims 2 and 6 define compounds of Formula (I) with R1 is (optionally substituted) heterocycle or (optionally substituted) heteroaryl for use in the treatment of microbial infections **with the added proviso**, that when R1 is (optionally substituted) 3-indolyl and R2 and R3 when taken together along with the carbon atom they are attached to form an (optionally substituted) aryl, an (optionally substituted) heteroaryl or an (optionally substituted) heterocyclyl then said microbial infection is a fungal infection.
Use- and method claims 14 and 17 as well as composition claim 22 contain the same proviso.
The application documents as filed do not contain any disclosure, that indolyl-substituted compounds of formula (I) may possess varying activities towards bacteria or fungi depending on the structure of R2 and R3. The proviso-amendment hence introduces subject-matter into the application documents for which no basis can be found in the application documents as filed, contrary to the requirements of Art. 41(2) PCT.
For the purposes of this Preliminary Examination, said provisos thus are disregarded, in accordance with Rule 70.2 (c) PCT.

V Reasoned statement with regard to novelty, inventive step and industrial applicability.

1). With respect to the **novelty** of the claimed compounds/compositions or their preparation the following **preliminary remarks** are made:
It is pointed out, that an intended purpose or use does not render a compound or composition novel with respect to known compounds or compositions comprising such compounds which in their chemical structure or formulation are essentially identical with the claimed compounds (PCT Guidelines 1998, Section IV, Ch. IV-7.6).
In case the terminology "for use as an (antimicrobial, antibacterial or antifungal) agent" is intended to define a 'first medical use'-type of claim, it is pointed out, that various documents already disclose such a use for 2,4,5-substituted imidazole compounds/compositions. A further medical use hence does not render such compounds/compositions novel.
Moreover, the terminology "for use as an antimicrobial (...) agent" is not unequivocally restricted to a medical or therapeutic use. It also includes, for example, agrochemical or disinfectant uses. It is evident from claim 4 that such a use is within the scope as envisaged by the present claims.
Claim 27 essentially defines a compound which does not differ from the compounds as defined by claims 1 - 12. A compound normally does not change its structure when

combined with another compound. 2nd Medical use OK Anti-microbial composition OK ?

2). **Validity of priority**

The priority document of the present application does neither disclose imidazole compounds of Formula (I) in which R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle or substituted heteroaryl nor the compounds of formulae VI or VII.
For these embodiments of the claims the priority date of 19.08.02 hence has not been validly claimed (see also PCT International Preliminary Examination Guidelines of October 1998, Section IV, Ch. V-2.3).

WO 03/00403 A1 (= D3) was published on 16.01.03, which is before the international filing date of the present application (19.08.03), and hence belongs to the prior art for these embodiments (Rule 64.1 (b) (i) and (ii) PCT).

D3 discloses benzimidazole compounds within the scope of present formula (I) in which R2 and R3 taken together with the carbon atoms they are attached to form a phenyl ring, exemplifying 2-(3-indolyl-)benzimidazoles in examples 45 and 64, and the use of such compounds for the treatment of diseases associated with microgiglia activation which include inflammatory diseases associated with bacterial infections (D3: page 21, line 16 - 19). D3 further discloses pharmaceutical formulations comprising such benzimidazole derivatives.
D3 hence anticipates the novelty of the compounds as defined by claims 2 - 4, 6 - 12 and 27 in which R2 and R3 when taken together along with the carbon atoms they are attached to, form an aryl or substituted aryl moiety and R1 is (optionally substituted) heterocycle or (optionally substituted) heteroaryl as well as the use of such compounds for the preparation of an antimicrobial composition as defined by claim 14 and antimicrobial compositions comprising such compounds as defined by claim 22 (Art. 33(2) PCT).

4). **Novelty**

a). The subject-matter of present claims 1 - 15, 17 - 22 and 27 furthermore is not novel (Art. 33 (2) PCT) with respect to the following documents:

- WO 00/78761 A1 (= D1) discloses 2-(3-indolyl-)substituted imidazole (especially benzimidazole) compounds for treating bacterial infections which are within the scope of compounds of formula (I) in which R2 and R3 when taken together along with the carbon atoms they are attached to, form an (optionally substituted) aryl moiety and R1 is (optionally substituted) heterocycle or (optionally substituted) heteroaryl as well as the use

of such compounds for the preparation of an antimicrobial composition as defined by claim 14 and antimicrobial compositions comprising such compounds as defined by claim 22. See in particular general structure I of D1 (page 18 and claims 1 and 21) and the specific compounds in Figures 1 - 10.
D1 also discloses, that these indolyl substituted benzimidazoles may be combined with further antimicrobial compounds (D1: page 42, line 19 - 23).
D1 thus anticipates the novelty of claims 2 - 4, 6 - 12, 14, 15, 17 - 20, 22 and 27.

- EP 77 024 A2 (= D2) discloses anti-inflammatory and antiallergic 2-heterocyclyl-3,5-diphenyl imidazole compounds within the scope of formula (I) as defined in claims 2 and 6 and pharmaceutical compositions comprising such compounds.
D2 hence anticipates the subject-matter of claims 2 - 4, 6 - 12, 22 and 27.

- WO 02/46168 A1 (= D4) discloses 2-(aryl/heteroaryl)-benzimidazole compounds for use as estrogen receptor ligands and (the preparation of) pharmaceutical compositions comprising these compounds (D4: page 14, line 6 - 23).
D4 hence anticipates the subject-matter of claims 1 - 14, 21, 22 and 27

- US 4,721,670 (= D5) discloses 2-((optionally substituted) pyrrolyl or indolyl)-4,5-di(optionally substituted)-aryl (phenyl)-imidazole compounds within the scope of formula (I) as defined in claim 2. See D5: formula (I) and the exemplified compounds starting from col. 3, line 36 onwards.
D5 hence anticipates the novelty of the compounds as defined by present claims 2, 4, 6, 8 - 12 and 27 insofar as the indicated use is for non-therapeutic purposes.

- WO 98/27065 A1 (= D6) discloses protein tyrosine phosphatase modulating compounds for therapeutic and diagnostic uses comprising 2-(substituted aryl/heterocyclyl)-4,5-di-(substituted) phenyl-imidazoles within the scope of formula (I) as defined by present claims 1 and 2 (D6: formula (A6) on pages 20/21 and specified compounds of Tables 3 - 6).
D6 furthermore discloses that these compounds may be used in pharmaceutical preparations for the treatment of disorders associated with microbial infections such as Yersinia bacteria (D6: paragraph bridging pages 29 and 30; page 99, last paragraph - page 101, last paragraph)
D6 hence anticipates the novelty of the compounds as defined by claims 1 - 12 and 27 as well as the use of such compounds for the preparation of a composition as defined by claims 13 and 14 and the compositions as defined by claims 21 and 22.

JP 11-199 582 A (= D7) discloses 2-((optionally substituted) heteroaryl/-cyclyl)-4-indolyl-5-

4-alkoxyphenyl-imidazoles to be used for the improvement of brain and central nervous functions.
D7 hence anticipates the novelty of the compounds of present claims 2 - 4, 6 - 12 and 27 as well as the (preparation of) the compositions as defined by claims 14 and 22.

Işikdağ et al., 1995 (= D8) disclose 2-(optionally substituted) phenyl-4,5-di- (optionally substituted) phenyl-imidazole compounds having an inhibitory activity on tubifex parasitical worms.
D8 hence anticipates the novelty of the compounds as defined by present claims 1, 3 - 5, 7 - 12 and 27.

WO 93/14081 A1 (= D10) discloses 2-(aryl/heteroaryl)-4-heteroaryl-5-aryl-imidazoles as anti-inflammatory compounds for treating diseases associated with excessive or unregulated cytokine production, including sepsis and septic shock, and pharmaceutical formulations comprising these compounds (D10: page 2, from line 5 onwards; page 21, line 21 - page 22, line 35).
D10 also discloses that these compounds are useful in the treatment of viral infections (D10: page 22, line 36 - page 23, line 18).
D10 hence anticipates the subject-matter of claims 1 - 14, 21, 22 and 27.

b). A method of inhibiting the growth and/or proliferation of a microbial cell by contacting that cell with a compound of formula (I) as defined in claim 16 has not been disclosed in the available prior art.
2-(3-indolyl)-imidazole compounds of formula (II) as defined by claim 23 and the 2-(3-indolyl)-4,5-diphenyl-imidazole compounds of formula (III) as defined in claim 24 have not been disclosed in the available prior art either. The used disclaimers clearly distinguish these compounds from the known indolyl-substituted compounds as e.g. disclosed in D2 and D5 - D7.
Compounds of formulae (VI) and (VII) as defined by claims 25 and 26, respectively, have not been disclosed either.

The subject-matter of claims 16 and 23 - 26 hence is novel (Art. 33 (2) PCT.

5). **Inventive step**
The subject-matter of claims 16 and 23 - 26 differs from that of the closest prior art, which is defined by D1, in the use of 2-aryl-imidazole compounds and/or 2-indolyl-imidazoles as defined by claims 23 - 26, for inhibiting the growth and/or proliferation of microbial cells instead of the 2-indolyl-benzimidazoles as used in D1.

The problem underlying the application thus can be seen as to provide further microbicidal imidazole compounds.
Examples 27 - 31 of the present application demonstrate, that the compounds as defined by formulae (VI) and (VII) and as used in the method of claim 16 solve this problem.
It has not been disclosed or suggested in the documents of the prior art, that the compounds as defined by claims 23 - 26 would possess these advantageous properties.

A method of inhibiting the growth of microbial cells by the compounds of formula (I) as defined in claim 16 has not been disclosed or suggested in the available prior art either and hence is considered inventive.

Insofar as the method of claim 17 is clearly and unequivocally distinguished from the method of D1 (i. e. by using a compound of formula (I) in which R2 and R3 are not taken together with the carbon atoms they are attached to), this method also would be considered to be based on an inventive step.

6). For the assessment of the present claims 16 and 17, insofar as they relate to a method of therapeutic treatment, on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for **first use** in medical treatment and the use of such a compound **for the manufacture of a medicament for a new medical treatment.**

Further deficiencies
Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 - D3, D5 and D6 is not mentioned in the description, nor are these documents identified therein.

value provided is against all 8 strains of *S. aureus* tested except where indicated otherwise. Table 4 shows the MIC values of 3 compounds selected as examples against other gram-positive bacteria, including 2 strains resistant to the first line antibiotic vancomycin.

5

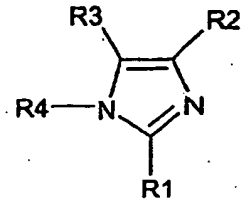
Table 3

Compound	MIC (µg/ml)
2	8-16
5	>128
7	4-16
9	8
11	8
13	2-4
15	>128
17	16[1]
19	4
21	8-16
23	4-8
25	32-64
27	32-64
29	>128
31	4
33	4-8
35	8
38	>128
40	>128
42	4
44	8
6	4
8	2
10	4

Compound	MIC(μg/ml)
20	2-4
26	2
28	2^2
32	8
34	>128
36	2
39	>128
41	>128
43	4
45	0.5
48	4-8
50	>64
51	16
52	>64
53	1
54	2-4
55	2
56	1
37	>128
46	4
49	4
83	>128
57	16
58	4
59	32
60	64
61	8
62	2
63	2

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A compound having structural formula (I):



(I)

wherein:

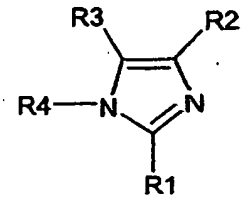
R1 is aryl, or substituted aryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano,

for use as an anti-microbial agent, wherein said compound has anti-microbial activity.

2. A compound having structural formula (I):



(I)

wherein:

R1 is heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

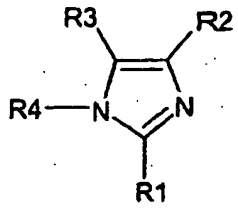
for use as an anti-microbial agent, wherein said compound has anti-microbial activity;

with the proviso that when R1 is 3-indolyl or substituted 3-indolyl, and R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl then said compound is for use as an anti-fungal agent.

3. The compound according to claim 1 or 2, wherein said anti-microbial agent is for the treatment or prevention of a microbial infection in an animal in need thereof.

4. The compound according to claim 1 or 2, wherein said anti-microbial agent is formulated for incorporation into a cosmetic product, personal care product, cleanser, polish, paint, spray, soap, or detergent.

5. A compound having structural formula (I), or a salt thereof:



(I)

wherein:

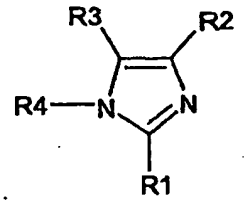
R1 is aryl, or substituted aryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

for use in the treatment or prevention of a microbial infection, wherein said microbial infection is a bacterial or fungal infection and said compound has anti-bacterial and/or anti-fungal activity.

6. A compound having structural formula (I), or a salt thereof:



(I)

wherein:

R1 is heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

for use in the treatment or prevention of a microbial infection, wherein said microbial infection is a bacterial or fungal infection and said compound has anti-bacterial and/or anti-fungal activity;

with the proviso that when R1 is 3-indolyl or substituted 3-indolyl, and R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl then said microbial infection is a fungal infection.

7. The compound according to claim 5 or 6, wherein said microbial infection is associated with a disease or disorder.

8. The compound according to any one of claims 5, 6, or 7, wherein said compound of structural formula I is used in combination with one or more anti-microbial agent(s).

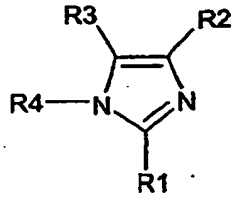
9. The compound according to any one of claims 5, 6 or 7, wherein said microbial infection is a bacterial infection.

10. The compound according to any one of claims 5, 6 or 7, wherein said microbial infection is a fungal infection.

11. The compound according to claim 9, wherein said bacterial infectionis is a Corynebacterium xerosis, Chlamydia pneumoniae, Chlamydia trachomatis, Enterobacter cloacae, Enterobacter faecalis, Enterococcus faecium, Escherichia coli, Escherichia coli O157:H7, Haemophilus influenzae, Helicobacter pylori, Listeria monocytogenes, Moraxella catarrhalis, Neisseria gonorrhoae, Neisseria meningitidis, Pseudomonas aeruginosa, Pneumococci species, Salmonella enterica, Salmonella typhimurium, Staphylococcus aureus, Staphylococcus aureus K147, Staphylococcus epidermidis, Staphylococcus typhimurium, Streptococcus mitis, Streptococcus pneumoniae, Streptococcus pyogenes, Vibrio cholerae, Mycobacterium tuberculosis, Mycobacterium africanum, Mycobacterium avium-intracellulare, Mycobacterium pneumoniae, Mycobacterium bovis, Mycobacterium leprae, Mycobacterium. phlei or Bacillus anthracis infection:

12. The compound according to claim 10, wherein said fungal infection is a Histoplasma, Coccidioides, Blastomyces, Paracoccidioides, Cryptococcus, Aspergillus, Zygomycetes, Basidiobolus, Conidiobolus, Rhizopus, Mucor, Absidia, Mortierella, Cunninghamella, Saksenaea, Candida, *Cryptosporidium parvum, Sporothrix schenckii, Piedraia hortae, Trichosporon beigelii, Malassezia furfur, Phialophora verrucosa, Fonsecae pedrosoi, Madurella mycetomatis* or *Pneumocystis carinii* infection.

13. Use of one or more compounds having structural formula (I), or a salt thereof, in the preparation of an anti-microbial composition:



(I)

wherein:

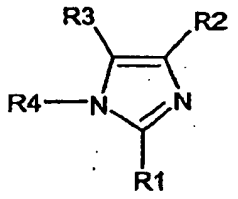
R1 is aryl,or substituted aryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

wherein said anti-microbial composition is an anti-bacterial or anti-fungal composition and said one or more compounds have anti-bacterial and/or anti-fungal activity.

14. Use of one or more compounds having structural formula (I), or a salt thereof, in the preparation of an anti-microbial composition:



(I)

wherein:

R1 is heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl and

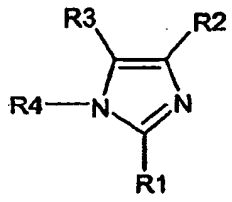
R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

wherein said anti-microbial composition is an anti-bacterial or anti-fungal composition and said one or more compounds have anti-bacterial and/or anti-fungal activity;

with the proviso that when R1 is 3-indolyl or substituted 3-indolyl, and R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, then said anti-microbial composition is an anti-fungal composition.

15. The use according to claim 14, wherein said anti-microbial composition further comprises one or more anti-microbial agent(s).

16. A method of inhibiting the growth and/or proliferation of a microbial cell comprising contacting said microbial cell with an effective amount of one or more compounds having general formula (I), or a salt thereof:



(I)

wherein:

R1 is aryl, or substituted aryl;

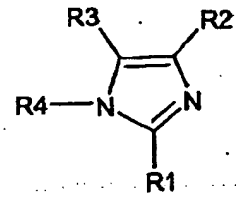
R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl,

substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

wherein said one or more compounds have anti-microbial activity.

17. A method of inhibiting the growth and/or proliferation of a microbial cell comprising contacting said microbial cell with an effective amount of one or more compounds having general formula (I), or a salt thereof:



(I)

wherein:

R1 is heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl;

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted

heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

wherein said one or more compounds have anti-microbial activity;

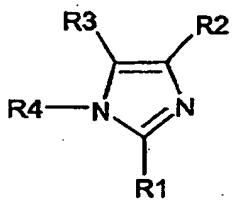
with the proviso that when R1 is 3-indolyl or substituted 3-indolyl, and R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, then said microbial cell is a fungal cell.

18. The method according to claim 16 or 17, further comprising contacting said cell with one or more anti-microbial agent(s).

19. The method according to any one of claims 16, 17 or 18, wherein said microbial cell is a bacterial cell and said one or more compounds have anti-bacterial activity.

20. The method according to any one of claims 16, 17 or 18, wherein said microbial cell is a fungal cell and said one or more compounds have anti-fungal activity.

21. An anti-microbial composition comprising an effective amount of one or more compounds having strucural formula (I), or a salt thereof, and a carrier, diluent or excipient:



(I)

wherein:

R1 is aryl, or substituted aryl;

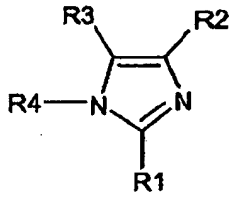
R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken

together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

wherein said anti-microbial composition is an anti-bacterial or anti-fungal composition and said one or more compounds have anti-bacterial and/or anti-fungal activity.

22. An anti-microbial composition comprising an effective amount of one or more compounds having strucural formula (I), or a salt thereof, and a carrier, diluent or excipient:



(I)

wherein:

R1 is heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl;

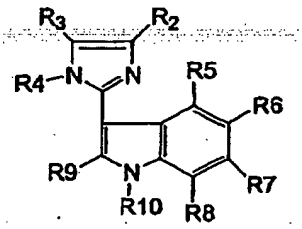
R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl or R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, and

R4 is hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

wherein said anti-microbial composition is an anti-bacterial or anti-fungal composition and said one or more compounds have anti-bacterial and/or anti-fungal activity;

with the proviso that when R1 is 3-indolyl or substituted 3-indolyl, and R2 and R3 when taken together along with the carbon atoms they are attached to, form aryl, substituted aryl, heterocycle, substituted heterocycle, heteroaryl, or substituted heteroaryl, then said anti-microbial composition is an anti-fungal composition.

23. A compound having the structural formula:



II

or a salt thereof, wherein:

R2 and R3 are independently aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, or substituted heteroaryl;

R4, R5, R6, R7, R8 and R9 are independently selected from hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted

heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

R10 is H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl, $-CH_2$-aryl, $-CH_2$-heteroaryl;

with the proviso that the compounds are other than:

3,3'-[5-(4-methoxyphenyl)-1H-imidazole-2,4-diyl]bis-1H-indole;

4,5-Bis(4-methoxyphenyl)-2-(3-indolyl)imidazole;

3-(4,5-diphenyl-1H-imidazol-2-yl)-1-methyl-1H-indole;

3-[4-(4-chlorophenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-bromophenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-methylphenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-methoxyphenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-ethoxyphenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4,5-bis (4-methoxydiphenyl)-1H-imidazol-2-yl)-1-methyl-1H-indole;

4,4'-[2-(2-phenyl-1H-indol-3-yl)-1H-imidazole-4,5-diyl]bis[N,N-dimethyl]benzenamine;

4,4'-[2-(5-chloro-1H-indol-3-yl)-1H-imidazole-4,5-diyl]bis[N,N-dimethyl]benzenamine;

2-(3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(3-indolyl)-4,5-bis[4-(diethylamino)phenyl]imidazole;

2-(2-phenyl-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(2-chloro-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(2-ethylcarboxylate-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(5-chloro-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

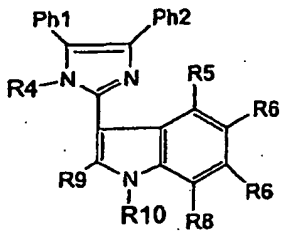
2-(5-cyano-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(5-nitro-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(5-ethylcarboxylate-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole; and

when R4 to R9 are H, and R10 is CH_3, then R2 and R3 are not both phenyl substituted at para position with –CH=CH-COOH or –CH=CH-COO-*t*-Bu.

24. A compound having the structural formula:



III

or a salt thereof, wherein:

Ph1 and Ph2 are independently selected from phenyl and substituted phenyl;

R4, R5, R6, R7, R8 and R9 are independently selected from hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

R10 is H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl;

with the proviso that the compounds are other than:

4,5-Bis(4-methoxyphenyl)-2-(3-indolyl)imidazole;

3-(4,5-diphenyl-1H-imidazol-2-yl)-1-methyl-1H-indole;

3-[4-(4-chlorophenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-bromophenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-methylphenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-methoxyphenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4-(4-ethoxyphenyl)-5-phenyl-1H-imidazol-2-yl]-1-methyl-1H-indole;

3-[4,5-bis (4-methoxydiphenyl)-1H-imidazol-2-yl)-1-methyl-1H-indole;

4,4'-[2-(2-phenyl-1H-indol-3-yl)-1H-imidazole-4,5-diyl]bis[N,N-dimethyl]benzenamine;

4,4'-[2-(5-chloro-1H-indol-3-yl)-1H-imidazole-4,5-diyl]bis[N,N-dimethyl]benzenamine;

2-(3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(3-indolyl)-4,5-bis[4-(diethylamino)phenyl]imidazole;

2-(2-phenyl-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(2-chloro-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(2-ethylcarboxylate-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(5-chloro-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

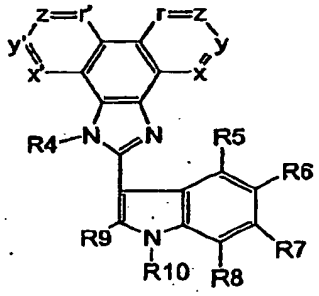
2-(5-cyano-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(5-nitro-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole;

2-(5-ethylcarboxylate-3-indolyl)-4,5-bis[4-(dimethylamino)phenyl]imidazole; and

when R4 to R9 are H, and R10 is CH_3, then Ph1 and Ph2 are not both phenyl substituted at para position with –CH=CH-COOH or –CH=CH-COO-*t*-Bu.

25. A compound having the structural formula:



VI

or a salt thereof, wherein:

R4, R5, R6, R7, R8 and R9 are independently selected from hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

R10 is H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl;

x is CR11 or N;

y is CR12 or N;

z is CR13 or N;

r is CR14 or N;

x' is CR15 or N;

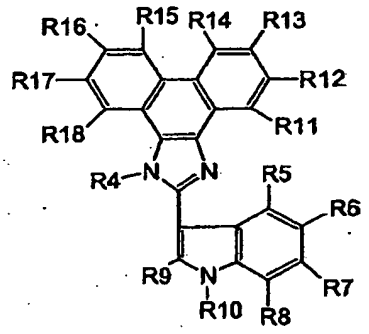
y' is CR16 or N;

z' is CR17 or N;

x' is CR18 or N;

R11, R12, R13, R14, R15, R16, R17 and R18 are independently selected from hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkenyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano.

26. A compound having the structural formula:



VII

or a salt thereof, wherein:

R4, R5, R6, R7, R8 and R9 are independently selected from hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, lower alkenyl,

substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano;

R10 is H, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, acyl;

R11, R12, R13, R14, R15, R16, R17 and R18 are independently selected from hydrogen, halogen, hydroxyl, thiol, lower alkyl, substituted lower alkyl, alkenyl, alkenyl, alkylalkenyl, alkyl alkynyl, alkoxy, alkylthio, acyl, aryloxy, amino, amido, carboxyl, aryl, substituted aryl, heterocycle, heteroaryl, substituted heterocycle, heteroalkyl, cycloalkyl, substituted cycloalkyl, alkylcycloalkyl, alkylcycloheteroalkyl, nitro, or cyano.

27. The compound according to any one of claims 1 to 12, wherein said compound is used in combination with one or more compounds of formula (I).